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Authors

Schuckit, Marc A
Smith, Tom L
Danko, George
et al.

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A 22-Year Follow-Up (Range 16 to 23) of Original Subjects with Baseline Alcohol Use Disorders from the Collaborative Study on Genetics of Alcoholism

Marc A. Schuckit, Tom L. Smith, George Danko, John Kramer, Kathleen K. Bucholz, Vivia McCutcheon, Grace Chan, Samuel Kuperman, Victor Hesselbrock, Danielle M. Dick, Michie Hesselbrock, Bernice Porjesz, Howard J. Edenberg, John I. Nureberger Jr., Marcy Gregg, Lara Schoen, Mari Kawamura, Lee Anne Mendoza

Background: Recent reports indicate higher-than-expected problematic drinking in older populations. However, few data describe how to predict which older individuals are most likely to demonstrate alcohol-related problems, including those with earlier alcohol use disorders (AUDs). These analyses evaluate predictors of alcohol outcomes in individuals with earlier AUDs in the Collaborative Study on Genetics of Alcoholism (COGA).

Methods: Original COGA participants with baseline AUDs at about age 40 were interviewed 13 to 26 years later and placed into clinically derived outcome categories. Chi-square and analysis of variance evaluated baseline differences across 4 outcome groups, with significant items entered into binary logistic regression backwards elimination analyses predicting outcomes.

Results: Low-Risk Drinkers (N = 100) at follow-up were predicted by baseline higher levels of response to alcohol (high LRs), lower histories of alcohol treatment, experience with fewer types of illicit drugs, and were more likely to have been widowed. At follow-up, Problem Drinkers (N = 192) differed from High-Risk Drinkers (N = 93) who denied multiple alcohol problems by exhibiting baseline lower LRs, higher Sensation Seeking, and a higher proportion who were widowed. Abstinent (N = 278) outcomes were predicted by a history of higher baseline AUD treatments, higher alcohol problems, lower usual drinks, as well as older age and European American heritage. Thirty-four subjects (4.9%) could not be classified and were not included in these analyses.

Conclusions: These results generated from AUD individuals from both treatment and nontreatment settings reinforce low probabilities of recent Low-Risk Drinking in individuals with AUDs, but also suggest many individuals with AUDs demonstrate good outcomes 2 decades later.

Key Words: Alcohol, Geriatrics, Prediction, Longitudinal.

ALCOHOL PROBLEMS, INCLUDING alcohol use disorders (AUDs), are likely to begin in the late teens to early 20s and often persist into older age (Brennan et al., 2011; Grant et al., 2018; Schuckit, 2017). Although alcohol consumption and problems usually decrease as drinkers grow older (Knott et al., 2018), this trend has been less obvious in the recent decade where the proportion of individuals age 65 and older who drank increased by 20% and there was a 2-fold increase in AUDs (Grant et al., 2018). Older drinkers carry additional risks because they develop higher blood alcohol concentrations (BACs) per drink, have greater brain sensitivity to alcohol's effects, and display enhanced risks for alcohol-related medical problems and accidents (Bjork et al., 2008; Breslow et al., 2017; Grant et al., 2018; Moore et al., 2007; Schuckit and Smith, 2013; Shield et al., 2018; Vestal et al., 1977).

Relatively little is known about drinking patterns decades later for older persons with earlier AUDs (Falk et al., 2010; Gastfriend et al., 2007). One potential desirable outcome for any age-group is Abstinence, which is a goal for most AUD treatment programs, especially for people with alcohol dependence (Center for Behavioral Health Statistics and Quality, 2014; Probst et al., 2015), although this is a relatively narrow perspective on recovery. Another positive outcome involves extended periods of nonproblem drinking with quantities consumed that conform to National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines for Low-Risk Drinking (McCutcheon et al., 2017; Witkiewitz et al., 2017a,b). On the other hand, adverse outcomes

From the Department of Psychiatry (MAS, TLS, GD, MG, LS, MK, LAM), University of California, San Diego, La Jolla, California; University of Iowa (JK, SK), Iowa City, Iowa; Washington University (KKB, VM), St. Louis, Missouri; University of Connecticut (GC, VH, MH), Farmington, Connecticut; Virginia Commonwealth University (DMD), Richmond, Virginia; State University of New York (BP), Brooklyn, New York; and Indiana University School of Medicine (HJE, JIN), Indianapolis, Indiana.

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Reprint requests: Marc A. Schuckit, MD, Department of Psychiatry, University of California, San Diego, 8950 Villa La Jolla Dr., Suite B-218, La Jolla, CA 92037; Tel.: 858-822-0880; Fax: 858-822-1002; E-mail: mschuckit@ucsd.edu

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include exceeding Low-Risk Drinking limits in the absence of multiple alcohol problems (High-Risk Drinking), and drinking associated with multiple problems (Problem Drinking). Both of these adverse outcomes are likely to be associated with potentially serious health problems and early death (Holahan et al., 2010; Kendler et al., 2016; Moore et al., 2007; Shield et al., 2018).

Regardless of the outcome, the fluctuating intensity of AUDs over time and the >20% spontaneous remission for AUDs (Schutte et al., 2006; Upah et al., 2015) contribute to the importance of longer term follow-ups (Cunningham et al., 2000; Schutte et al., 2006; Witkiewitz, 2008). Some of the longest published follow-ups of heavy drinkers and those with AUDs used mortality data as the ultimate adverse outcome (Haver et al., 2009; Kendler et al., 2016; Lundin et al., 2015); however, these evaluations rarely included baseline predictors. Studies that included a wider range of baseline predictors of outcomes often involved relatively modest-sized samples, focused on trajectories over time rather than predictors of individual outcomes, and/or used secondary analyses of other samples that often had limited available baseline information (Gonçalves et al., 2017; Jacob et al., 2009; Penick et al., 2010; Upah et al., 2015; Vaillant, 2003).

Baseline demographic characteristics that have predicted better outcomes (e.g., Abstinence and Low-Risk Drinking) include being currently married and living with a spouse, higher education and socioeconomic status, being employed, and active involvement with religion (Dawson et al., 2012; Edens et al., 2008; Mann et al., 2005; Timko et al., 2006). In contrast, adverse AUD outcomes have been associated with earlier and more intense involvement with alcohol, smoking or illicit drug use, higher rates of baseline alcohol problems, and histories of prior alcohol treatment (Brennan et al., 2011; Bucholz et al., 2017; Holahan et al., 2017; Smith et al., 1983; Timko et al., 2006). It should be noted, however, that histories of past alcohol treatments have also been associated with higher rates of future Abstinence (Dawson et al., 2012; Trim et al., 2013), perhaps reflecting reports that, for some individuals, more severe problems might precipitate alcohol treatments that, in turn, might contribute to better outcomes (Brennan et al., 2011; Trim et al., 2013).

Another predictor of future alcohol-related outcomes involves a person's need for a higher number of drinks to achieve desired effects beginning early in their drinking career (Schuckit and Smith, 1996; Schuckit et al., 1997, 2007, 2008). This phenomenon, which might reflect lower alcohol sensitivity per drink and/or acute intrasession tolerance (Schuckit, 2018), has been known since the 1970s as a low level of response, or low (LR), to alcohol. Low LRs correlate with higher alcohol quantities per occasion even in relatively light drinkers as young as age 12, and before intersession, tolerance was likely to have developed (Schuckit et al., 2008). In addition, among individuals who develop AUDs, a lower LR might also be associated with a greater chance of Abstinence or Low-Risk Drinking recoveries (Gonçalves et al., 2017; Trim et al., 2013). This might reflect the absence of a strong relationship between a lower LR and other risk factors cited as increasing both the risk for and severity of AUDs, including high levels of impulsivity and Sensation Seeking that might impact on a more severe AUD course (Fein et al., 2010; Littlefield et al., 2009; Penick et al., 2010; Schuckit and Smith, 2017; Smith et al., 1983). Another predictor of outcomes relates to greater stimulation effects of alcohol especially at rising BACs (e.g., King et al., 2016).

Two recent studies using different populations of older individuals with AUDs reported that between 16% and 22% denied multiple alcohol problems as defined by the DSM-IV (American Psychiatric Association, 1994) and were drinking at or below low-risk levels for at least the prior year (low-risk Drinking). In these studies, 6% to 36% exceeded Low-Risk Drinking limits but denied experiencing AUD problems (High-Risk Drinking); 38% to 63% reported DSM AUD items the year before follow-up (Problem Drinking), while 9% and 10% reported recent alcohol Abstinence (Gonçalves et al., 2017; McCutcheon et al., 2017).

In these studies, significant predictors of Low-Risk Drinking included female sex, older age, and higher LRs (greater alcohol sensitivity), as well as lower baseline alcohol intake and problems, less smoking and illicit drug use, lower rates of seeking help for mental health problems, and lower Novelty Seeking. At the other end of the spectrum, an Abstinent outcome was predicted by older age, European American (EA) heritage, lower education, low LRs, high baseline drinking parameters, illicit drug use, and smoking, along with a high likelihood of seeking mental health treatment and high Novelty Seeking. The authors speculated that it was possible that the similarity between predictors of Abstinence and Problem Drinking outcomes might reflect the fact that predictors of adverse drinking outcomes could predispose a drinker to more problems if they continue to drink, which might then bring the person to a decision that they needed to stop drinking overall. Predictors of the 2 outcomes of High-Risk Drinking with and without continued alcohol problems did not differ dramatically, as both outcomes related to higher proportions of subjects with EA heritage, low LRs, and high baseline drinking parameters (Gonçalves et al., 2017).

The current analyses go beyond these recent papers by focusing on 4 clinically based outcome categories observed an average of 2 decades later in a large group of men and women with AUDs at baseline. Similar detailed drinking-related follow-up data could not be generated for deceased subjects, and, consequently, those individuals are the focus of a separate paper. Based on prior work (Gonçalves et al., 2017; McCutcheon et al., 2017), the analyses were structured to evaluate 5 hypotheses. Hypothesis 1 predicted that, based on our prior studies and additional data (Helzer et al., 1985), follow-ups carried out several decades later will show that <20% of these subjects will report recent Low-Risk Drinking. Hypothesis 2, also based on our prior studies, stated that recent Low-Risk Drinking would be predicted by a pattern of baseline characteristics that included lower alcohol use

parameters and higher sensitivity to the effects of alcohol (a high LR; the opposite of a low LR to alcohol), less drug use and problems, as well as lower indications of externalizing characteristics regarding conduct problems, Novelty Seeking, and Sensation Seeking. Reflecting the finding of Gonçalves and colleagues (2017), Hypothesis 3 predicted similarities between subjects who recently consumed alcohol above Low-Risk Drinking levels but denied multiple alcohol-related problems and drinkers who admitted to recent alcohol-related difficulties regarding demography, LR, baseline drinking parameters, illicit drug use, Novelty Seeking, and Sensation Seeking. Hypothesis 4 predicted that Abstinence at follow-up would relate to a baseline pattern of older age, more alcohol and drug problems, and a higher probability of having received prior AUD-related treatments, with more problems and subsequent treatment associated with the probability that the person will select Abstinence as their way to deal with their AUD. Finally, based on an earlier finding in younger subjects (Trim et al., 2013), Hypothesis 5 predicted that high LRs would be associated with Low-Risk Drinking and High-Risk Drinking in the absence of multiple alcohol problems and that low LRs would be associated with multiple alcohol problems and Abstinence in the period before follow-up.

MATERIALS AND METHODS

Overview and Baseline Data

This study is the initial step in future plans to locate and carry out extensive evaluations with all available Collaborative Study on Genetics of Alcoholism (COGA) subjects enrolled in the first phases of our protocol, including a battery of electrophysiological measures. The first step in that process was to select a subsample from the >10,000 participants and demonstrate that they can be located, determine the proportion still alive, describe the alcohol-related outcomes for the survivors, and evaluate their willingness to participate in future follow-ups.

Beginning in 1990 and following approval from Human Subjects' Protections Committees at all 6 COGA data collection sites, original probands and their relatives were assessed with the valid and reliable Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) interview (Bucholz et al., 1994; Hesselbrock et al., 1999). Data at study entry (i.e., baseline) included current demography, standard drink-based quantities (as defined below) and drinking frequencies for the prior 6 months, lifetime histories of alcohol problems, lifetime mental health histories, childhood and adolescent conduct problems, as well as current scores for the Tridimensional Personality Questionnaire (TPQ), Novelty Seeking Questionnaire (Cloninger et al., 1991), and the Zuckerman Sensation Seeking Questionnaire (Zuckerman, 1996). Data were also gathered using the Self-Rating of the Effects of Alcohol (SRE) measure regarding the number of standard drinks (12 g ethanol as seen in 12 oz beer, 4 oz of nonfortified wine, or a single "shot" of whiskey, gin, or similar beverages) required for up to 4 effects of alcohol, including first feeling any effect, slurring speech, feeling unsteady when walking, and unwanted falling asleep. The average drinks needed for those effects the approximate first 5 times of drinking produced the SRE5 score; and the average drinks across the first 5 times, the period of heaviest drinking, and the recent 3 months was used to produce the SRE Total (SRET) score (Ray et al., 2011; Schuckit, 2018; Schuckit et al., 2007). The SRE alphas are 0.90, and up to 5-year retest reliabilities are 0.66 (Ray et al., 2011; Schuckit et al., 1997). The SRE5 was developed as a potential measure of a person's sensitivity and/or intrasession tolerance to alcohol very early in their drinking careers, and before intersession, tolerance was likely to have developed. The SRET was structured to include reactions to alcohol during periods of heavier drinking that might point toward the development of intersession tolerance. For the SRE, higher average drinks required for effects indicate lower LR values per drink.

Follow-Up Subject Selection and Recruitment

The data presented here were generated from recent interviews with the selected COGA subjects described below, each of whom had given informed consent for future contact. Sample selection for this phase of the study was affected by the limited funding, which precluded extensive evaluations of all COGA participants. Reflecting the major goal for this phase of the work of describing the drinking status of older individuals who had AUDs earlier in life, recruitment was limited to participants whose current age was 50 years and older. Consistent with the plan to begin to search for gene variations potentially related to AUD outcomes, this phase was also limited to individuals for whom DNA samples had been collected in the past. Following these guidelines, we identified 663 subjects who met these criteria and were among our final sample of whom 38.8% were original probands with AUDs selected from alcohol treatment programs, 51.6% were probands' biological relatives (e.g., siblings) with AUDs, 3.5% were spouses with AUDs, and 6.2% were nonbiological relatives with AUDs (e.g., in-laws who married into the probands' families).

Subjects were located using information in their COGA records or through relatives participating in a current COGA protocol. They were then directly contacted, asked to give informed consent to participate, and scheduled for a telephone interview that, considering the limited payment that could be offered, was designed to take no longer than 20 minutes. Determination of death during the follow-up period was based on information from relatives and from a National Death Index search.

Follow-Up Interviews

The follow-up interview, for which subjects were paid $25, used a subset of questions modified from the SSAGA regarding demography as well as alcohol and drug quantities, frequencies, and problems. To keep the interview in this phase as short as possible, questions emphasized prior 5-year alcohol problems using a time frame a priori felt to be likely to be remembered for events that included alcohol-related blackouts, difficulties maintaining drinking limits, spending much time using or recovering from effects, interpersonal or work/school problems, use in hazardous situations, problems cutting back or stopping use, alcohol-related health impairment, and signs of alcohol withdrawal. Reflecting concerns regarding the time frame over which drinking quantities and frequencies would be likely to be remembered by individuals with AUDs in their 60s, these items were only queried regarding the 12 months prior to interview. Self-ratings of current physical and mental health were each scored on a 4-point scale from excellent to poor, and self-rating of memory on a 3-point scale of better, the same, or worse compared to other people their age.

Follow-Up Subject Participation

Among the 2,174 COGA initial probands who had been selected for follow-up, 2,149 had a baseline DSM-IV AUD diagnosis (American Psychiatric Association, 1994) at their first interview, of whom 512 were determined to have died and are the focus of a separate

paper. Of the remainder, 28 were located but were unavailable for further evaluation because they were incarcerated or too ill to be interviewed (e.g., severe dementia), 55 refused evaluation, and 697 were interviewed an average of 21.7 (SD 3.29) years after their initial COGA interview (range 13 to 26 years). Outcomes for an additional 857 individuals could not be determined within the year of data collection in this study. Thus, 1,292 of the 2,149 (60.1%) subjects were located (i.e., had died, were interviewed, were contacted but refused, or were located but could not be interviewed). Among the 1,554 COGA participants likely to be still alive and available for interview, 697 (44.9%) were interviewed. Among these, 34 were Abstinent the year prior to interview but had 2 or more alcohol problems in the 5 years prior to interview and who therefore did not fit into any of the outcome categories used in the analyses.

Data Analyses

Statistical comparisons were carried out across baseline data for those subjects for whom follow-up status was determined and the 857 eligible for follow-up but whose outcome could not be determined. At baseline, those not located were a bit younger (38.8 vs. 37.9), less likely to be female (44.0% vs. 34.1%) or EA (74.4% vs. 62.9%), a bit less educated (12.9 vs. 12.6 years), more likely to identify with a religion (83.6% vs. 86.3%), and had higher SRET scores (7.2 vs. 7.6). Those not followed also reported higher maximum drinks (24.5 vs. 26.1), and a higher proportion with illicit drug use (81.0% vs. 89.3%).

Interviewed subjects were placed into outcome categories using guidelines similar to those used in several recent follow-ups (Gonçalves et al., 2017; McCutcheon et al., 2017). Group 1 (Low-Risk Drinking) consumed alcohol the prior year, using quantities that never exceeded 3 standard drinks (about 12 g of ethanol) per day and 13 drinks per week, and denied 2 or more alcohol problems in the prior 5 years. Group 2 (High-Risk Drinking) in the past year had at least 1 occasion where they exceeded the Low-Risk Drinking guidelines but denied 2 or more alcohol problems in the prior 5 years. Group 3 (Problematic Drinking) admitted to 2 or more alcohol problems in the prior 5 years, and Group 4 (Abstinent) reported no alcohol consumption in the year prior to follow-up and denied having 2 or more alcohol problems in the prior 5 years.

Analyses began with comparisons across the 4 outcome groups regarding descriptions of their follow-up demography, alcohol use and problem patterns, and health status using chi-square for categorical data and analysis of variance for continuous variables, as shown in Table 1. A similar approach in Table 2 evaluated differences across the 4 groups regarding their baseline characteristics, with additional evaluations comparing Groups 2 (High-Risk Drinking) and 3 (Problem Drinking) to test Hypothesis 3. Subsequently, baseline predictors that were significantly different across the 4 groups in Table 2 were entered into binary backwards elimination regression analyses, using 1,000 bootstraps, predicting each outcome independently, as shown in Table 3. Regression analyses did not include items that overlapped greatly

Table 1. Outcome Characteristics for 663 Interviewed Original COGA Participants with DSM-IV AUDs Divided into 4 Clinically Derived Outcome Groups Based on Follow-Up Interviews

Group characteristics	All Ss (N = 663) M (SD) or %	Group 1 (Low-Risk Drinking) (n = 100, 15.1%) M (SD) or %	Group 2 (High-Risk Drinking) (n = 93, 14.0%) M (SD) or %	Group 3 (Problem Drinking) (n = 192, 29.0%) M (SD) or %	Group 4 (Abstinent) (n = 278, 41.9%) M (SD) or %	F or χ^2
Current demography						
Age (years)	60.5 (7.92)	62.4 (9.40)	59.0 (6.94)	58.0 (5.86)	62.2 (8.34)	15.44***
Sex (% female)	44.0	55.0	45.2	41.7	41.7	6.07
Race (% EA)	73.9	72.0	80.6	66.1	77.2	10.17*
Education (years)	13.3 (2.08)	13.6 (2.08)	13.5 (2.18)	13.0 (1.98)	13.3 (2.09)	2.22
Marital status (% yes)						
Married	47.8	52.0	48.4	40.6	50.6	30.08***
Divorced/separated	30.4	28.0	35.5	38.5	24.7	
Widowed	9.0	16.0	5.4	5.2	10.3	
Never married	12.8	4.0	10.8	15.6	14.4	
Currently employed (% yes)	48.9	56.0	58.1	46.4	45.5	7.07
Prior year drinking						
Maximum drinks/occasion	7.7 (6.43)	2.1 (0.76)	6.5 (3.33)	11.3 (6.85)	na	229.30***
Usual drinks/wk	13.6 (15.78)	2.4 (2.01)	10.7 (11.44)	21.0 (17.61)	na	99.02***
Usual frequency/wk	3.3 (2.47)	1.7 (1.46)	3.4 (2.45)	4.1 (2.51)	na	37.68***
Prior 5-year problems						
Number of alcohol problems[a]	2.4 (2.55)	0.1 (0.35)	0.5 (0.50)	4.4 (2.04)	na	783.76***
Current health status						
Physical health[b]	2.4 (0.82)	2.3 (0.75)	2.2 (0.75)	2.6 (0.81)	2.3 (0.84)	6.33***
Mental health[b]	2.0 (0.76)	2.0 (0.74)	1.9 (0.68)	2.1 (0.76)	1.9 (0.78)	3.16*
Memory[b]	1.9 (0.64)	1.9 (0.63)	1.9 (0.56)	2.0 (0.67)	1.9 (0.65)	0.58
Number of health problems	1.4 (1.23)	1.4 (1.20)	1.1 (1.04)	1.5 (1.34)	1.4 (1.21)	2.32

DSM, Diagnostic Statistical Manual; AUDs, alcohol use disorders; EA, European American; COGA, Collaborative Studies on Genetics of Alcoholism; Ss, subjects; Low-Risk Drinking, prior year drinking but <4 standard drinks (12 g ethanol)/d and <14 drinks/wk and <2 alcohol problems prior 5 years; High-Risk Drinking, >drink limits for Low-Risk Drinking and <2 alcohol problems prior 5 years; Problem Drinking, 2+ alcohol problems prior 5 years; Abstainer, no alcohol use prior 5 years; na, not applicable.

[a]Alcohol problems listed in text.

[b]Higher score = worse outcome.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table 2. Baseline Characteristics for 663 COGA Original Participants with DSM-IV AUDs Divided into 4 Clinically Derived Outcome Groups

Group characteristics	All Ss (N = 663) M (SD) or %	Group 1 (Low-Risk Drinking) (n = 100, 15.1%) M (SD) or %	Group 2 (High-Risk Drinking) (n = 93, 14.0%) M (SD) or %	Group 3 (Problem Drinking) (n = 192, 29.0%) M (SD) or %	Group 4 (Abstinent) (n = 278, 41.9%) M (SD) or %	All 4 groups F or χ^2	Groups 2 (High-Risk Drinking) versus Group 3 (Problem Drinking) F or χ^2
Baseline demography							
Age (years)	38.8 (8.02)	40.1 (9.26)	37.3 (7.19)	36.6 (6.28)	40.4 (8.45)	10.44***	ns
Sex (% female)	44.0	55.0	45.2	41.7	41.4	6.17	na
Race (% EA)	74.4	72.0	80.6	66.1	78.8	11.86**	6.38*
Education years	12.9 (2.07)	13.1 (2.04)	13.2 (1.88)	12.8 (1.94)	12.8 (2.22)	1.44	ns
Religion (% yes)	83.6	90.0	82.8	80.7	83.5	4.18	na
Marital status (% yes)[a]							
Married	56.9	54.0	63.4	54.2	57.6	19.77*	ns
Divorced/separated	34.1	36.0	29.0	39.2	31.7		
Widowed	1.4	5.0	0.0	1.0	0.7		
Never married	7.7	5.0	7.5	5.7	10.1		
Baseline alcohol characteristics							
SRE first 5 (SRE5)	4.5 (2.00)	4.2 (2.12)	4.0 (1.72)	4.6 (2.01)	4.6 (2.00)	3.23*	7.55**
SRE total (SRET)	7.2 (2.96)	6.2 (2.76)	6.4 (2.60)	7.6 (2.86)	7.6 (3.08)	10.53***	12.94***
Lifetime family history AUD (%)	37.6	39.0	38.7	41.1	34.2	2.55	na
Maximum drinks/occasion (6 month)	24.6 (10.40)	20.6 (10.33)	21.1 (9.62)	25.0 (10.00)	26.6 (10.33)	12.39***	9.69**
Usual drinks/occasion (6 month)	5.9 (7.09)	4.1 (5.97)	5.2 (5.38)	7.8 (6.99)	5.5 (7.74)	23.54***	ns
Usual frequency/wk (6 month)	3.0 (2.76)	2.3 (2.42)	3.1 (2.58)	3.9 (2.60)	2.4 (2.87)	13.04***	5.50*
Age onset AUD	24.0 (7.18)	24.4 (7.88)	23.2 (6.37)	24.0 (6.77)	24.2 (7.47)	0.35	ns
Number of alcohol problems (lifetime)	6.9 (2.51)	5.8 (2.39)	5.8 (2.52)	6.8 (2.54)	7.6 (2.27)	20.18***	9.10**
Ever alcohol treatment (% yes)	62.6	41.0	44.1	64.6	75.2	52.65***	10.80***
Drug characteristics							
Ever smoke (% yes)	66.5	67.0	59.1	62.5	71.6	6.88	na
Ever illicit drug use (% yes)	81.0	69.0	79.6	88.5	80.6	16.61***	4.10*
Number of drug types ever used	3.7 (2.90)	2.4 (2.45)	3.5 (2.92)	4.2 (2.79)	3.8 (2.99)	9.12***	ns
Any drug Dx ever (% yes)	60.2	47.0	54.8	66.7	62.2	12.25**	ns
Number of drug problems (lifetime)	6.9 (9.26)	4.4 (7.78)	5.3 (7.68)	7.6 (9.68)	7.8 (9.74)	6.55***	4.26*
Mental health and personality							
Mental health Rx ever (% yes)	67.4	61.0	65.6	64.1	72.7	6.48	na
Depression Dx ever (% yes)	18.1	22.0	18.3	13.0	20.1	5.15	na
Any conduct item yes	93.7	92.0	93.5	92.7	95.0	1.56	na
Number of conduct items to age 15	3.4 (2.22)	2.8 (1.94)	3.1 (2.00)	3.6 (2.36)	3.5 (2.25)	3.24*	ns
TPQ Novelty Seeking	17.1 (4.79)	16.1 (4.72)	16.7 (5.48)	17.4 (4.22)	17.5 (4.90)	2.53	ns
Zuckerman Sensation Seeking	17.0 (6.01)	15.2 (5.08)	16.6 (5.60)	18.7 (6.10)	16.7 (6.14)	8.96***	8.19**

Abbreviations include those defined in Table 1 plus SRE, Self-Rating of the Effects of Alcohol; SRE5, average number of standard drinks for effects the approximate first 5 times of drinking on the SRE; SRET, SRE average values across first 5, heaviest drinking, and recent 3-month periods; Dx, diagnosis; TPQ, Tridimensional Personality Questionnaire; Rx, treatment; Depression Dx, diagnosed DSM-IV major depressive disorder; alcohol problems, number of DSM-IV alcohol use disorder criteria; ns, not significant; na, not applicable for Group 2 versus 3 comparisons because the variable was not significantly different across the 4 outcome groups.

[a]Follow-up analyses: only widowed significantly different across the 4 groups.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table 3. Series of Binary Logistic Regression Backwards Elimination Analyses Where Each Group is Compared with the Other 3 Groups as Well as Group 2 versus Group 3 (Odds Ratio with 95% Confidence Intervals)

Out group	Group 1 (Low-Risk Drinking) (n = 100, 15.1%)	Group 2 (High-Risk Drinking) (n = 93, 14.0%)	Group 3 (Problem Drinking) (n = 192, 29.0%)	Group 4 (Abstinent) (n = 278, 41.9%)	Group 2 (High-Risk Drinking) versus Group 3 (Problem Drinking)[a]
Baseline variables					
Demography					
Age (years)			0.76 [0.62, 0.92]**	1.38 [1.16, 1.64]***	
Race (% EA)			0.51 [0.34, 0.76]***	1.74 (1.17, 2.58)**	0.42 [0.23, 0.78]**
Marital status (% widowed)	6.89 [1.68, 28.24]**				
Alcohol characteristics					
SRE first 5 (SRE5)		0.76 [0.60, 0.96]*			
SRE total (SRET)	0.72 [0.56, 0.92]**				1.57 [1.17, 2.10]**
Usual drinks/occasion (6 months)		1.44 [1.11, 1.67]**	1.79 [1.45, 2.20]***	0.58 [0.49, 0.69]***	
Usual frequency/wk (6 months)					
Number of alcohol problems (lifetime)				1.42 [1.16, 1.73]***	
Ever alcohol treatment (% yes)	0.50 [0.31, 0.79]**	0.40 [0.25, 0.63]***		2.32 [1.52, 3.54]***	
Drug characteristics					
Number of drug types ever used	0.64 [0.50, 0.84]***				
Number of drug problems (lifetime)					
Mental health and personality					
Number of conduct items to age 15					
Zuckerman Sensation Seeking			1.43 [1.18, 1.73]***		1.42 [1.08, 1.88]*
Pseudo-R^2	0.13	0.07	0.17	0.22	0.12

[a]Dependent variable here = Group 3 (Problem Drinking).
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ for the results of the backwards elimination analysis.
Abbreviations are defined in Tables 1 and 2.

with other variables (e.g., omitting a DSM-IV diagnosis when the number of DSM items was entered).

Nonindependence was not a problem for this sample as the design effects were small (1.00 to 1.43) regarding 17 of the key variables evaluated, reflecting the fact that 388 of 440 families (88.2%) had only 1 or 2 individuals in these analyses (Muthén and Satorra, 1995). Missing data were handled with maximum likelihood procedures as they were missing at random (Little's Missing Completely at Random test x^2 = 869.440, df = 1,077, p = 1.00). Data transformations (log, square root, and inverse) were used when appropriate. For the regression analyses, continuous variables were z-scored with the result that odds ratios are comparable across groups.

Outcome group assignment followed the criteria outlined in Materials and Methods to produce 4 outcome groups for the total of 663 participants who could be classified by this approach. Outcomes included the following: (i) consistent with Hypothesis 1, the group with Low-Risk Drinking in the year before follow-up in the absence of multiple alcohol problems in the prior 5 years included 100 subjects (15.1% of those classified); (ii) participants with prior year High-Risk Drinking without multiple drinking problems in the prior 5 years included 93 individuals (14.0%); (iii) Problem Drinking in the prior 5 years included 192 individuals (29.0% of those classified); and (iv) Abstainers for the prior year in the absence of multiple alcohol problems in the 5 years before follow-up included 278 participants (41.9%).

RESULTS

Table 1 describes the characteristics at follow-up for the 4 groups. As shown in the overall summary in the first data column of Table 1, at follow-up the average age for these 663 individuals was 60 years, 44% were female, 74% were of EA heritage, these participants had on average 13 years of education, and about half were currently employed. At the time of interview, almost half were married, a third were divorced, 9% were widowed, and 13% were single (never married). These interviewed subjects rated both their current physical and mental health to be on average good (scored as 2 on a 4-point scale from excellent to poor) and estimated their current memory to be about the same as most people their age (scored as a 2 on a 3-point scale of better/same/worse).

Focusing on Table 1 characteristics at follow-up that were significantly different across outcome groups, consistent with how Group 1 was defined, at follow-up these subjects reported the lowest drinking quantities and frequencies and the lowest average number of alcohol problems. Low-Risk Drinking Group 1 members were also among the oldest at follow-up and among the most likely to be married. High-Risk Drinking Group members indicated drinking parameters that were between those of the other 2 groups who reported drinking at follow-up and had the highest proportion of EA individuals. Participants in the Problem Drinking Group reported the highest alcohol use parameters among the 3 drinking groups along with the worst values for current physical and mental health (higher scores indicate worse outcomes), and had the lowest proportion of EAs. Abstinent subjects were relatively older, had relatively higher proportions of EAs, and were the least likely to be currently divorced or separated from a spouse.

Table 2 describes relationships to the outcome categories for baseline characteristics when evaluated across the 4

groups, and Table 3 demonstrates results of binary logistic regression backwards elimination analyses incorporating variables with significant differences across groups in Table 2. In Table 3, predictors of each outcome are evaluated in comparison with the combined remaining groups, along with a direct comparison of Problem Drinkers with High-Risk Drinkers to address Hypothesis 3.

Focusing on baseline items with significant differences across outcome groups, regarding Hypothesis 2 alcohol-related items for Low-Risk Drinking participants included relatively low SRE values (high LRs per drink), the lowest baseline drinking quantities and frequencies, among the lowest baseline number AUD items endorsed, and a low proportion with baseline histories of AUD-related treatments. Low-Risk Drinkers also reported the lowest rates for all illicit drug-related items and had the lowest number of conduct problems, Novelty Seeking, and Sensation Seeking. Regarding demography, participants in Group 1 were a bit older, had a lower proportion of subjects with EA heritage, and were more likely to be widowed. In Table 3, participants with Low-Risk Drinking (Pseudo-R^2 = 0.13) demonstrated low SRET scores (indicating a high LR or greater alcohol sensitivity) were unlikely to have had prior AUD treatments, reported experience with fewer illicit drug categories, and were more likely to have been widowers at baseline.

Hypothesis 3 proposed that there would be few differences in predictors between High-Risk Drinkers and Problem Drinkers in Groups 2 and 3. However, the data in the last column of Table 2, directly comparing baseline characteristics across these groups, indicated that, compared to High-Risk Drinkers, members of the Problem Drinking Group had higher SRE scores (lower LRs per drink), higher baseline maximum drinking quantities and frequencies, reported more alcohol problems, and were more likely to have had prior AUD treatment. Problem Drinkers were also more likely to have ever used illicit drugs at baseline, had higher numbers of substance use disorder (SUD) problems, reported higher Sensation Seeking scores, and were less likely to be EA. This pattern of differences across Low-Risk and High-Risk Drinkers was supported by the regression analysis in Table 3 that demonstrated that Problem Drinkers had higher SRET and Sensation Seeking scores and were less likely to be EA.

Relevant to Hypothesis 4, the univariate analyses in Table 2 indicated that at baseline Abstinent Group members had relatively high SRE5 and SRET values (low LRs), high maximum drinks per occasion, relatively lower usual drinks (especially in relation to the value for the Problem Drinking Group), a higher number of DSM AUD items endorsed, and were the most likely to have had histories of prior AUD treatments. These members of Group 4 reported using among the highest number of types of illicit drugs, were more likely than most other groups to carry a drug diagnosis, endorsed the highest number of DSM SUD criterion items, reported relatively high numbers of conduct problems, and had relatively high Sensation Seeking. Members of the Abstinent Group were also older and the most likely to have an EA heritage. In the regression analysis in Table 3 (Pseudo-R^2 = 0.22), Abstinent participants were predicted by baseline lower usual drinks, a higher number of alcohol problems, greater experience with prior AUD treatments, as well as older age and EA heritage.

Regarding Hypothesis 5, considering the data in Tables 2 and 3, as predicted a lower number of drinks needed for effects (high LR per drink) were related to future Low-Risk Drinking and to High-Risk Drinking in the absence of multiple alcohol problems. Conversely, high SRE scores (low LR per drink) were related to Problem Drinking and Abstinent outcomes.

DISCUSSION

This study presents results of the largest and longest prospective follow-up of individuals with AUDs for whom detailed baseline information had been gathered by the same research group almost 2 decades earlier. The current protocol is the first step in preparing for a more costly and intensive study of a broader group of COGA participants, including those without AUDs and comparison subjects. In this step, the data gathered over a 1-year period demonstrated subjects could be found, death outcomes could be established, 95% of located subjects agreed to be interviewed, and all interviewees agreed to future follow-ups. The data gathered allowed for analyses to evaluate 5 hypotheses regarding potential baseline predictors of 4 a priori established outcome categories.

Hypothesis 1 proposed that <20% of the participants would demonstrate Low-Risk Drinking in the prior year in the absence of multiple alcohol problems over the prior 5 years, and only 14% of these subjects fulfilled criteria for this Low-Risk Drinking category. The results are consistent with several other papers evaluating outcomes for individuals with AUDs (Gonçalves et al., 2017; Helzer et al., 1985; McCutcheon et al., 2017). Hypothesis 2 proposed that Low-Risk Drinking would be predicted by earlier lower SRE scores (high LRs per drink), low alcohol and drug involvement, and low externalizing characteristics. The univariate analyses in Table 2 confirmed most of those predictions, with the greatest salience in the Table 3 regression analysis observed for a high LR (i.e., a low number of drinks required for effects on the SRE), the absence of prior AUD treatments, experience with fewer illicit drugs, and having been widowed at baseline. LR status contributed to predictions of several outcomes and is commented on below, the absence of prior AUD treatments might reflect a less severe course of AUDs before baseline, and the low drug experiences might reflect lower externalizing characteristics. The salience of being widowed at baseline was not hypothesized and might reflect the role of stresses in the course of the AUDs for these individuals. Clinically relevant take-home messages from these data include the following: (i) 12-month Abstinence is not the only way to characterize positive alcohol outcomes in

older drinkers with AUDs; (ii) Low-Risk Drinking occurs but is not the usual outcome for individuals with AUDs who continue alcohol consumption; and (iii) sustained Low-Risk Drinking is most likely for individuals with relatively modest levels of alcohol and drug problems and higher LRs.

Based on recent findings in individuals with higher educational achievement (Gonçalves et al., 2017) as well as the prediction that High-Risk Drinkers might underreport alcohol problems, Hypothesis 3 proposed that predictors of High-Risk and Problem Drinking Groups would be similar. However, in Table 3 Problem Drinkers had higher SRE scores (lower LRs per drink), had higher Sensation Seeking, and were less likely to have an EA heritage. In univariate analyses in Table 2, Problem Drinkers also had higher baseline maximum quantities, drinking frequencies, alcohol problems, illicit drug use, and drug problems. The greater difference between these 2 groups in COGA versus more white-collar individuals in the Gonçalves and colleagues (2017) study could reflect moderation of the course of Problem Drinking by higher levels of education and socioeconomic factors in the earlier study (Bucholz et al., 2017; McCutcheon et al., 2014). Even though the outcome and baseline problems were not as severe for High-Risk Drinking participants, it is important to remember high alcohol consumption still carries a greater risk for alcohol-related health problems (Breslow et al., 2017; Grant et al., 2018; Moore et al., 2007; Praud et al., 2016; Shield et al., 2018).

Table 3 also shows supported elements of Hypothesis 4 regarding the role of baseline alcohol problems and prior AUD treatment as well as older age as predictors of Abstinence. In Table 2, univariate analyses also offered support for lower LR (higher drinks for effects on the SRE), baseline higher maximum drinks, and higher drug involvement (e.g., the higher number lifetime drug problems). Consistent with Hypothesis 4 and supported by prior papers using different groups of subjects (Gonçalves et al., 2017; McCutcheon et al., 2017), these findings might reflect a more severe course of their AUD for members of Group 4, which might be related to a greater propensity to either stop drinking on their own or enter Abstinent-oriented treatment programs. An exception to this pattern is the relatively low usual drinks per occasion, which probably reflected the relatively higher value for this variable for the Problem Drinking Group. The pattern of more severe alcohol problems at baseline predicting later Abstinence is also consistent with several prior papers (Brennan et al., 2011; Holahan et al., 2017; Smith et al., 1983; Timko et al., 2000).

The proportion of individuals with recent Abstinence in the current study (42%) was higher than the 10% with Abstinence in our follow-ups of COGA relatives and in the 25-year follow-up of men from the San Diego Prospective Study (Gonçalves et al., 2017; McCutcheon et al., 2017). Those disparate proportions might reflect the older age of the current subjects, where Abstinence at an average of 60 requires survival to that age, and 24% of subjects selected for follow-up were deceased and are the focus of another paper. Perhaps individuals with AUDs who are followed into their 60s might have demonstrated continued alcohol problems in their 40s and 50s but be most likely to survive into their 60s if they achieved Abstinence. The different rates of Abstinence might also relate to the current long follow-up period that gives additional opportunity for spontaneous remission that has been reported to occur in more than 20% of individuals with AUDs (Schutte et al., 2006; Upah et al., 2015).

Consistent with Hypothesis 5, high LRs (needing fewer drinks for effects on the SRE) were related to more benign alcohol outcomes, perhaps because more feedback from fewer drinks might make it easier to stop drinking during an evening (Schuckit and Smith, 1996; Schuckit et al., 2007, 2008; Trim et al., 2013). On the other hand, a lower LR per drink (more drinks needed for effects on the SRE) was associated with both Problem Drinking and Abstinent Groups in Table 2. The relationship of LR to the Abstinent Group might reflect both the heavy drinking likely to contribute to the decision to stop consuming alcohol and the fact that LR is not closely related to impulsivity (Schuckit and Smith, 2017). Higher impulsivity is likely to interfere with treatment responses and to increase the probability of returning to heavier drinking (Littlefield et al., 2010). A lower number of drinks needed for effects (a higher LR per drink) might also have contributed to the greater ability of High-Risk Drinkers, compared to Problem Drinkers, to avoid multiple alcohol problems. The contributions by LR to predicting outcomes were observed even after considering age, sex, as well as drinking and drug use histories in the same analyses, indicating that LR may have added unique information for predicting later outcomes. The fact that both SRE5 (potentially relating to levels of reaction to alcohol early in the career and before acquired intersession tolerance is likely to have developed) and SRET (a measure that is likely to include both initial sensitivity and acquired tolerance) contributed to differentiating between outcome groups is also of interest, although the fact that these 2 measures were not always concordant is a reminder that they are likely to measure related, but not identical phenomena (Schuckit, 2018).

Some additional findings worthy of comment include noting that religious involvement, which was not related to outcomes here but had been reported in some other studies (Dawson et al., 2012), might be most important over relatively modest periods of time but have less salience to long-term outcomes in individuals in their 60s and beyond. Also, the interview questions regarding the categories of living as married and married were asked a bit differently at baseline and follow-up, a differential that might have contributed to differences in subjects who reported themselves as never married across baseline and follow-up interviews. Regarding other demographic characteristics, however, our current findings are consistent with our 2 recent reports that indicated higher proportions of individuals with EA heritage in the Abstinent Group and lower proportions in the High-Risk Drinking and the alcohol problem outcomes (Gonçalves et al., 2017; McCutcheon et al., 2017).

As with all research, it is important to recognize caveats that apply to the current work. First, although the sample is relatively large and the follow-ups were on average 2 decades, during the year of data collection outcomes were determined for only 60% of the subset of COGA subjects selected for analysis, and only 45% of those eligible were interviewed during the year of data collection (Munafò et al., 2017). Thus, although the current results resemble several other recent reports (Gonçalves et al., 2017; McCutcheon et al., 2017), the data presented here need to be reevaluated in the planned more intense follow-up of a much larger COGA sample. Second, because the data presented here required personal interviews with participants regarding recent drinking practices and problems, deceased subjects could not be included in the current analyses, and predictors of death and specific death causes are the subject of a separate paper. Third, all data were from self-reports without corroborating information. A fourth caveat is inherent in the COGA data set where the original families were selected based on a proband who was in alcohol-related treatment and had multiple relatives with AUDs. Therefore, this is not an epidemiological study of individuals with AUDs in the general population (Grant et al., 2015). These considerations indicate that the results might not be representative of all individuals with AUDs and might be different in less severely impaired individuals without alcoholic close relatives. Fifth, reflecting concerns regarding what events are likely to be most accurately remembered, details of drinking quantities and frequencies were limited to the 12 months preceding the follow-up interview, while major drinking problems were recorded regarding the prior 5 years. Sixth, although age differences across groups were relatively small and age was included in regression analyses, it is possible that some of the differences across outcome groups could reflect differences in age. Finally, the COGA baseline data available as predictors of outcome categories did not include other valuable variables such as the greater alcohol-related stimulation early in the blood alcohol curve.

In conclusion, this study reports predictors of recent drinking outcomes in individuals identified as having an AUD at about age 40 who were followed up at an average age of 60. The results support the low probability that these individuals with AUDs would be able to drink within the NIAAA guidelines for Low-Risk Drinking for 12 months and in the absence of multiple alcohol problems in the 5 years preceding follow-up. Results also reinforce the importance of distinguishing between High-Risk Drinking in the absence of multiple alcohol problems and Problem Drinking-related outcomes. Within this older population, 42% achieved and maintained Abstinence in the 5 years preceding follow-up.

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